UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/819,669	03/17/1997	THIERRY BOON	LUD-5253.5-D	1995

24972 7590 10/01/2002

FULBRIGHT & JAWORSKI, LLP
666 FIFTH AVE
NEW YORK, NY 10103-3198

EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/01/2002

42

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	08/819669	BOON
	Examiner	Art Unit
	GAMBEL	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 8/16/02

2a)☐ This action is **FINAL**. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 183-191

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 183-191

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☑ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Applicant's Status Request (Paper No. 41), filed 8/16/02, is acknowledged.

2. Claim 183-191 are pending

Claims 1-182 have been canceled previously.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Upon reconsideration of the file history of the instant application, New Grounds of Rejection are set forth herein.

5. Upon a review of the prosecution of the instant application, the following is noted.

Paper No. 32, stated that "Upon consideration of the Boon-Falleur / van der Bruggen / van den Eynde / Van Pel / De Plaen / Lurquin / Chomez Declaration under 37 C.F.R. § 1.132, filed 7/10/00 (Paper No. 30); the previous New Matter rejection under 35 U.S.C. § 112, first paragraph, and objection to under 35 U.S.C. 132, with respect to the current SEQ ID NOS: 7/8 have been withdrawn; given that the current SEQ ID NOS: 7/8 are based upon the same clones as that disclosed in the specification as filed."

However, applicant has not deposited the biological materials disclosed in the specification as filed, which provided for the re-sequencing the 1.7 / 1.8 cDNA molecules disclosed in the specification as filed.

Therefore, in the absence of satisfying the requirements under 35 U.S.C. 112, first paragraph, for the deposit of biological materials, claims 19-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons of record.

It is apparent that the original clones to re-sequence the 1.7 / 1.8 cDNA molecules disclosed in the specification as filed is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the appropriate clone. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

Applicant should clearly pont out that the clones relied upon in the Boon-Falleur / van der Bruggen / van den Eynde / Van Pel / De Plaen / Lurquin / Chomez Declaration under 37 C.F.R. § 1.132, filed 7/6/00 and 7/10/00 (Paper Nos. 33-35) are the same exact clones disclosed in the specification as filed.

6. Claims 183-191 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention essentially for the reasons of record and set forth herein.

The instant claims are drawn to isolated tumor rejection antigen precursor proteins wherein said protein is encoded by a nucleic acid molecule, the complementary sequence of which hybridizes to the nucleotide sequence as set forth in SEQ ID NO: 8.

Tumor antigen precursors are processed to form the presentation of tumor rejection antigens (page 2 of the specification), including but not limited to those most characteristic of a particular tumor (page 4 of the specification)

While the nucleic acid set forth in SEQ ID NO: 8 appears to code for the tumor rejection antigen precursor MAGE-1; there is insufficient information concerning the identifying structural and functional characteristics of nucleic acids of which complementary nucleic acids hybridize to SEQ ID NO: 8 under stringent conditions encoding a MAGE-1 tumor antigen precursor.

The specification discloses in Example 23 (page 19) that MAGE refers to a family of tumor rejection antigen precursors molecules which share a certain degree of homology. Example 25 (page 43) acknowledges that genes encoding MAGE-1,-2-3 cross hybridized to a considerable extent.

Further it is noted that Ding et al. (Biochem. Biophys. Res. Commun. 202: 549-555, 1994) disclose that homologous MAGE-1 can be polymorphic (see entire document, particularly page 551, paragraph 1).

Nucleic acids of which the complementary sequences hybridize to SEQ ID NO: 8 do not provide sufficient written description provision of 35 USC 112, first paragraph for a broad genus of diverse tumor rejection antigen precursors.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed tumor antigen precursor and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification fails to describe these DNA sequences.

The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Here, the specification does not provide sufficient written description of a tumor antigen precursors based upon the limited disclosure/recitation of a one nucleic acid encoding MAGE-1. There is insufficient written description of the structure / sequences of nucleic acids or which the complementary sequence can hybridize to SEQ I NO: 8 and encode a broad genus of diverse tumor antigen precursors and, in turn, provide the appropriate structural and functional attributes of a myriad of tumor antigen precursors, with distinct structural, expression and functional properties..

Further, given the polymorphism and homology of MAGE tumor antigen precursors; there is insufficient written description of the alternative or allelic forms of a tumor antigen precursor encoded by nucleic acids hybridizes to SEQ ID NO: 8 under the written description provision of 35 USC 112, first paragraph.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that this is a written description rejection rather than an enablement rejection under 35 U.S.C. 112, first paragraph.

7. Claims 183-191 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a MAGE-1 tumor antigen precursor encoded by SEQ ID NO: 8; does not reasonably provide enablement for any "an isolated nucleic acid ... the complementary sequence of which hybridizes under stringent conditions to SEQ ID NO: 8 wherein said isolated nucleic acid molecule codes for a tumor rejection antigen precursor".

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

While the recitation of "tumor antigen precursor" may have some notion of the properties of the claimed molecule(s), claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make and use the "tumor antigen precursors", commensurate in scope with the claimed invention.

"It is not sufficient to define the recombinant molecule by its principal biological activity, e.g. having protein A activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992).

As pointed out above; there is acknowledged polymorphism and homology among MAGE tumor antigens, including MAGE-1.

For example, it is noted that Ding et al. (Biochem. Biophys. Res. Commun. 202: 549-555, 1994) discloses that homologous MAGE-1 can be polymorphic (see entire document, particularly page 551, paragraph 1).

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases.

For example, Skolnick et al. (Trends in Biotech. 18:34-39, 2000) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36).

Similarly, Bork (Genome Research 10:398-400, 2000) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399).

Smith et al. (Nature Biotechnology 15:1222-1223, 1997) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene

There is insufficient guidance and direction as to how to make and use the breadth of nucleic acids encoding MAGE-1 tumor antigen precursors by hybridizing complementary sequences to SEQ ID NO: 8 alone; other than that encompassed by SEQ D NO: 8 in the absence of structural or functional attributes that define a MAGE-1 tumor antigen precursor.

Tumor antigen precursors are processed to form the presentation of tumor rejection antigens (page 6 of the specification), including but not limited to those most characteristic of a particular tumor (page 8 of the specification)

A person of skill in the art is not enabled to make and use the breadth of MAGE-1 tumor antigen precursors, which can be processed to form the presentation of tumor rejection antigens and be characteristic of a particular tumor, commensurate in scope with the claimed invention. The skilled artisan would not predict that all that is required for a tumor antigen precursor is that it can be encoded by a nucleic acid of which the complementary sequence hybridizes to SEQ ID NO: 8. A skilled artisan would expect that other structural and functional attributes would be required to provide for a nucleic acid to encode a MAGE-1 tumor antigen precursor and its ability to be processed to form a tumor rejection antigen characteristic of a particular tumor.

For example, a person of skill in the art could not predict which particular nucleic acids (or amino acid sequences) other than that was set forth in SEQ ID NO: 8 would be sufficient to confer the ability to encode a MAGE-1 tumor antigen precursor and, in turn, wherein the MAGE-1 tumor antigen precursor can be processed to form a tumor rejection antigen characteristic of a particular tumor

The claims are not even limited to MAGE-1 tumor antigen precursors.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, making and using tumor antigen precursors encoded by nucleic acids of which the complementary sequence hybridizes to SEQ ID NO: 8, wherein the appropriate structural and functional features of MAGE-1 tumor antigen precursor would be maintained would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

8. Applicant is reminded of the following.

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

The reference to USSN 07/764,364 in the oath appears in error, as this application issued as U.S. Patent No. 5,327,252 directed to a print apparatus.

Application Number 764,364 has the last "4" crossed out and "PCT/US92/04354 / 22 May 1992" has been crossed out.

It is noted that applicant's amendments, filed 6/30/00 (Paper No. 29) and 6/12/01 (Paper No. 38) indicate that applicant will address the defective oath upon allowance.

9. Again, while it is acknowledged that both "BALB/C" and "BALB/c" are used in the literature to describe this mouse strain; applicant is reminded that "BALB/c" is the proper designation of this mouse strain (see pages 27-28).

With respect to applicant's lack of understanding; applicant is invited to amend the specification to disclose the proper designation of this mouse strain in the instant application.

The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected

10. No claim allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
September 27, 2002